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	Examiner:	Sarah E. Perlinger
	Art Unit:	1625
	Attorney Docket No.	P-142-US1
From:	**Theravance, Inc.**	
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Date:	**August 10, 2006**	
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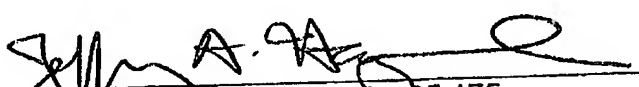
Signature :	
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Total Number of Pages in This Submission	10

Application Number	10/696,464
Filing Date	October 29, 2003
First Named Inventor	Mammen et al.
Art Unit	1625
Examiner Name	Sarah E. Perlinger
Attorney Docket Number	P-142-US1

ENCLOSURES *(check all that apply)*

- ☐ Fee Transmittal Form
  - ☐ Fee Attached
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  - ☐ After Final
  - ☐ Affidavits/declaration(s)
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- ☐ Certified Copy of Priority Document(s)
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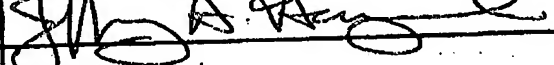
Signature			
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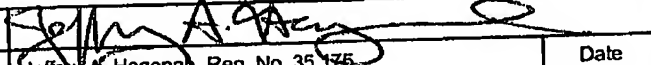
Signature			
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PATENT
Attorney Docket No. P-142-US1
Customer No. 27038

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	
MAMMEN et al.	Confirmation No. 5983
Application No.: 10/696,464	Group Art Unit: 1625
Filed: October 29, 2003	Examiner: Sarah E. Perlinger
For: SUBSTITUTED 4-AMINO-1-(PYRIDYLMETHYL)PIPERIDINE AND RELATED COMPOUNDS	

PETITION FROM REQUIREMENT FOR RESTRICTION
PURSUANT TO 37C.F.R. §1.144

Mail Stop Amendment
Commissioner for Patents
P. O. Box 1450
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Attn: Director, Technology Group 1600

Sir:

Applicants respectfully petition the Director to review of the requirement for restriction in the above-identified application. This petition is being filed on even date with a reply to the pending Office Action mailed on May 31, 2006.

I. BACKGROUND

In an Office Action mailed on March 20, 2006, the Examiner indicated that restriction to one of the following inventions was required under 35 U.S.C. §121:

Group I: Claims 1-33, 39 and 44-46 drawn to compound of formula I wherein p=1 and one of W, X, Y and Z is nitrogen or N->O, a pharmaceutical composition comprising a therapeutically effective amount of a compound of any of Claims 1-33 and a process for preparing a compound of formula I, classified in class 546 and various subclasses;

Group II: Claims 1-17, 20-24, 39 and 44-46 drawn to compound of formula I wherein p=1 and two of W, X, Y and Z are nitrogen or N->O, a pharmaceutical composition comprising a therapeutically effective amount of a compound of any of Claims 1-33 and a process for preparing a compound of formula I, classified in class 544 and various subclasses;

Group III: Claims 1-19, 39 and 44-46 drawn to compound of formula I wherein p=2 and one of W, X, Y and Z is nitrogen or N->O, a pharmaceutical composition comprising a therapeutically effective amount of a compound of any of Claims 1-33 and a process for preparing a compound of formula I, classified in class 546, subclasses 187-193;

Group IV: Claims 1-17, 39 and 44-46 drawn to compound of formula I wherein p=2 and two of W, X, Y and Z are nitrogen or N->O, a pharmaceutical composition comprising a therapeutically effective amount of a compound of any of Claims 1-33 and a process for preparing a compound of formula I, classified in class 544 and various subclasses;

Group V: Claim 34 drawn to a compound of formula IV, which is an intermediate of Group II, classified in various classes and subclasses;

Group VI: Claim 35 drawn to a compound of formula V, which is an intermediate of Group II, classified in various classes and subclasses;

Group VII: Claim 36 drawn to a compound of formula VI, which is an intermediate of Group III, classified in various classes and subclasses;

Group VIII: Claim 37 drawn to a compound of formula VII, which is an intermediate of Group IV, classified in various classes and subclasses;

Group IX: Claim 38 drawn to a compound of formula VIII, which is an intermediate of Group V, classified in various classes and subclasses;

Group X: Claims 40-43 drawn to a method for treating a mammal having a medical condition alleviated by treatment with a muscarinic receptor antagonist, classified in various classes and subclasses.

In a response filed on March 28, 2006, Applicants elected Group I with traverse in part. Specifically, Applicants traversed the requirement for restriction of Groups I-IV for the reasons of record in the March 28, 2006 response.

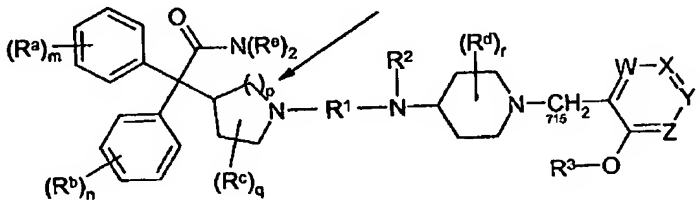
In a subsequent Office Action mailed May 31, 2006, the Examiner withdrew the requirement for restriction of Groups I and II; and Groups III and IV; but maintained the requirement for restriction of Groups I/II relative to Groups III/IV. This requirement for restriction was made FINAL.

II. REQUESTED ACTION

Applicants respectfully request review and reconsideration of the requirement for restriction of Groups I/II relative to Groups III/IV. If this petition is granted, Applicants respectfully request that Groups I-IV be rejoined and examined on the merits.

III. DISCUSSION

Groups I-IV are directed to compounds of formula I:



I

In Group I/II, *p* is 1; and in Group III/IV, *p* is 2. The arrow above shows the location of variable *p*. Groups I-IV also include pharmaceutical compositions comprising such compounds; and processes of preparing the compounds.

The basis for the restriction of Groups I/II relative to Groups III/IV is set forth in the Office Action mailed on May 31, 2006, as follows:

> ...the compounds of groups I and III-IV are classified separately as illustrated in the restriction requirement sent March 20, 2006 and it would be extremely burdensome to search such diverse core structures. Each independent core structure is classified separately and requires a separate search in the electronic database. Furthermore, compounds having the biphenyl piperdine carbamoyl core structure of the instant claimed compound can be utilized to treat conditions other than those delineated in the instant application and therefore, a reference anticipating or rendering obvious, one of the inventions of groups I and III-IV would not necessarily anticipate and/or render obvious, any of the other inventions of groups I-IV. Markush practice clearly delineates that for proper Markush grouping compounds of the group must (1) share a common utility, and (2) share a substantial structural feature essential to that utility (see MPEP 803.02, *In re Weber*, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and *In re Haas*, 580 F2d 461, 198 USPQ 334 (CCPA 1978). In the instant case, the biphenyl piperidine carbamoyl core has been disclosed to have utility for treating allergic disorders while the biphenyl pyrrolidine carbamoyl core is recognized in the art to have muscarinic antagonist activity, thus, a different utility (see Walsh et al., J. Med. Chem., 1989, 32, pages 105-118, especially page 109 compound 102 and page 108, compound 72). The lack of common core is proper for restriction and separate examination. Office Action at page 2.

In response, Applicants begin by noting that the Examiner's requirement for restriction has divided individual claims into separate restriction groups based on members in a Markush group. When determining whether such a restriction requirement is proper, it is important to begin with the general proposition that an applicant for a patent has a right to have each claim considered on the merits without the claim being "chopped up" into fragmentary claims by the examiner. This fundamental principle was clearly set forth in *In re Weber, Soder and Boksay* where the court stated:

> As a general proposition, an applicant has a right to have *each* claim examined on the merits. If an applicant submits a number of claims, it may well be that pursuant to a proper restriction requirement, those claims will be dispersed to a number of applications. Such action would not affect the right of the applicant eventually to have each of the claims examined in the form he considers to best define his invention. If, however, a single claim is required to be divided up and

> presented in several applications, that claim would never be considered on the merits. The totality of the resulting fragmentary claims would not necessarily be the equivalent of the original claim. Further, since the subgenera would be defined by the examiner rather than by the applicant, it is not inconceivable that a number of the fragments would not be described in the specification. *In re Weber, Soder, and Boksay*, 580, F.2d 455, 458-459, 198 U.S.P.Q. 328, 331-332 (C.C.P.A. 1978) (emphasis in original).

In view of this strong admonition by the court that applicants have a right to have each claim examined on the merits, MPEP §803.02 sets forth that it is improper to require restriction of the members of a Markush group unless the subject matter in the claim lacks unity of invention.

1. Examiner Has Not Established Lack of Unity of Invention

Unity of invention exists where compounds included within a Markush group (a) share a common utility and (b) share a substantial structural feature essential to that utility.

(a) Common Utility

The compounds of Groups I-IV share a common utility; for example, they are all muscarinic receptor antagonists. See, for example, page 51, lines 16-17 of the specification which states "[t]he substituted 4-amino-1-(pyridylmethyl)piperdine and related compounds of this invention are useful as muscarinic receptor antagonists...."

The Examiner has argued "the biphenyl piperidine carbamoyl core has been disclosed to have utility for treating allergic disorders while the biphenyl pyrrolidine carbamoyl core is recognized in the art to have muscarinic antagonist activity, thus, a different utility." For at least the following reasons, this argument is insufficient to establish a lack of common utility.

First, the standard for unity of invention is whether the compounds included within the Markush group **share a common utility**. Accordingly, it does not matter that some members of the Markush group might have a different utility so long as they share a

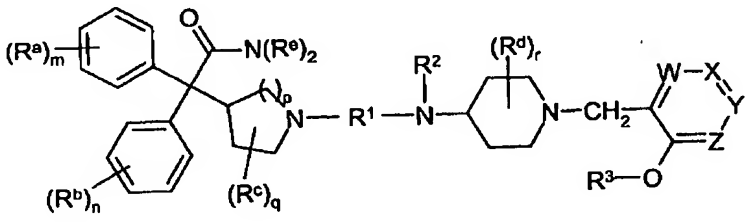
common utility. In the present case, the compounds of formula I share the common utility of being muscarinic receptor antagonists.

Additionally, the compounds cited by the Examiner as having a different utility (i.e., the biphenyl piperidine carbamoyl core disclosed in Walsh et al., J. Med. Chem., 1989, 32, pages 105-118) are not members of the present Markush group and therefore, their utility is irrelevant. The standard for unity of invention is whether **the compounds included within the Markush group** share a common utility. Thus, compounds not included in the present Markush group, such as those mentioned by the Examiner, are irrelevant to the analysis of unity of invention.

In this regard, it is particularly important to note that there are significant structural differences between the compounds mentioned by the Examiner (i.e., those disclosed in Walsh et al.) and the compounds of formula I in the present application. In view of these differences, it is not unexpected that such compounds might have different utilities. Thus, the utility of structurally different compounds, such as those mentioned by the Examiner, is irrelevant to the analysis of unity of invention for the present claims.

(b) Substantial Structural Feature

The compounds of Groups I-IV share a substantial structural feature essential for their common utility. Specifically, the compounds of these groups share the common structural features found in formula I:



I

As is readily apparent from this formula, compounds in which *p* is 1 share a substantial portion of their structure in common with compounds in which *p* is 2. Essentially, the only difference is one extra methylene unit (i.e, -CH_2-) in the compounds

where *p* is 2 (which methylene unit may be optionally substituted). Applicants' specification indicates that compounds of formula I are muscarinic receptor antagonists (see, for example, page 51, lines 16-17). Thus, the common core of the compounds of formula I provide such compounds with their utility as muscarinic receptor antagonists.

Accordingly, since the compounds in Groups I-IV share a common utility and a substantial structural feature essential to that utility, they do not lack unity of invention. Therefore, the requirement for restriction of Groups I-IV is improper and should be withdrawn.

2. No Serious Burden

In support of the requirement for restriction, the Examiner has also stated "the compounds of groups I and III-IV are classified separately as illustrated in the restriction requirement sent March 20, 2006 and it would be extremely burdensome to search such diverse core structures."

In response to this argument, Applicants respectfully note that the compounds of Groups I/II and III/IV differ essentially by only one carbon atom. Thus, contrary to the Examiner's statement, these groups do not represent "diverse core structures." While the historic PTO classification system may have placed pyrrolidine and piperidine ring systems in separate classes to aid in manual searching, modern electronic search tools readily permit permutations in ring size to be included in the same search and therefore, such ring systems can be searched together without serious burden.

M.P.E.P. § 803 states, in part, that "[i]f the search and examination of an entire application can be made without **serious** burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions." MPEP § 803 at 800-4 (emphasis added).

In the present case, the compounds of Groups I/II and III/IV share a substantial common core structure and differ essentially by only one carbon atom. Therefore, such compounds can be searched without serious burden. In this regard, Applicants respectfully note that the standard set forth by the M.P.E.P. guidelines is the imposition of a **serious** burden on the examiner not just an additional burden. The facts in the

present situation do not support a finding of a **serious** burden. Accordingly, the Examiner must examine these groups in their entirety on the merits even if they are independent or distinct inventions.

For the foregoing reasons, Applicants respectfully request that this petition be granted and Groups I-IV be rejoined and examined on the merits.

IV. FEES

No fees are believed to be due for submission of this petition. However, if a fee is due, the Commissioner is hereby authorized to charge the requisite fee, or to credit any overpayments, to Deposit Account No. 50-0344 (in the name of Theravance, Inc.).

V. CONCLUSION

Applicants respectfully request consideration of this petition. Should there be any questions regarding this petition, the Director is encouraged to call the undersigned attorney for Applicants at (650) 808-6406.

Respectfully submitted,
THERAVANCE, INC.

Date: August 10, 2006

By: _____
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